U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

4.351

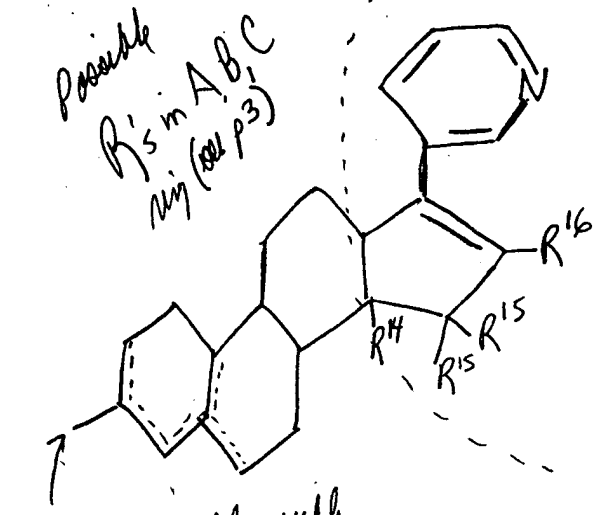
Requestor's Name: Bottino Serial Number: 08/315,882

Date: 4/22/96 Phone: 305-6335 Art Unit: 1202

Search Topic:

John Please

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



Possible R's in A, B, C ring (or p3)

HO
or
O=
CH_2=
C≡N
$-NO_2$

all possible double bonds

the only fixed & novel part is within the dotted line.

STAFF USE ONLY

Date completed: 4-25-96
Searcher: JOHN DANIZMAN
Terminal time: ~~12~~ 16
Elapsed time:
CPU time:
Total time: 26
Number of Searches: 5
Number of Databases: 5

Reg Butstaff

Search Site
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Type of Search
- ____ N.A. Sequence
- ____ A.A. Sequence
- ✓ Structure
- ____ Bibliographic

Vendors
- ____ IG Suite
- ✓ STN
- ____ Dialog
- ____ APS
- ____ Geninfo
- ____ SDC
- ____ DARC/Questel
- ____ Other

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STRUCTURE FILE UPDATES:  19 APR 96   HIGHEST RN 175414-60-5
DICTIONARY FILE UPDATES: 24 APR 96   HIGHEST RN 175414-60-5

TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 1995

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=>
=> D QUE L10
L5                STR
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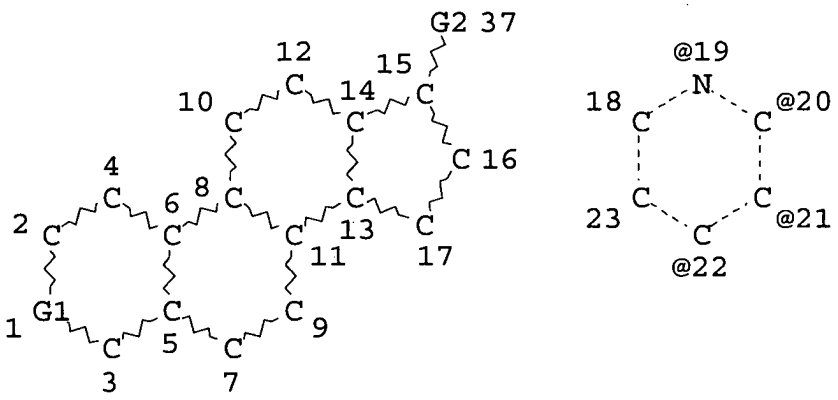


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CONNECT IS E1  RC AT  29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  32

STEREO ATTRIBUTES: NONE
L7          129 SEA FILE=REGISTRY SSS FUL L5
L9              STR
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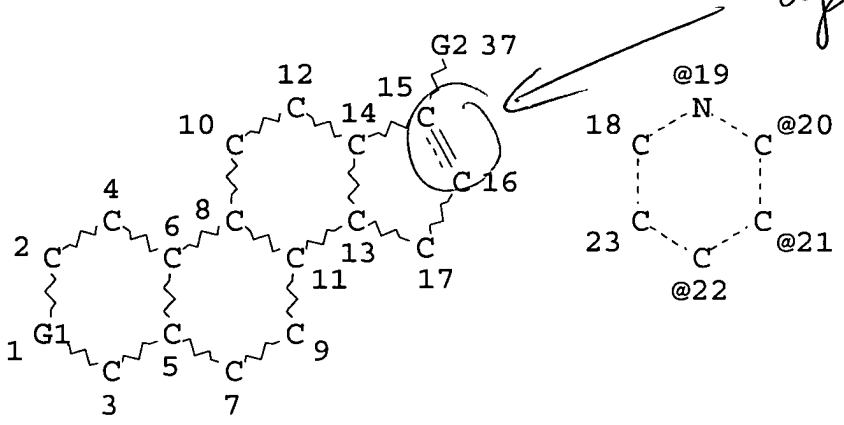
parent



Apparently this is novel

← Subset Search

CH2=C 26 @27 O~C 29 @30 NC~C 32 @33 O2N~C 35 @36

VAR G1=27/30/33/36
VAR G2=19/20/21/22
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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
L10 16 SEA FILE=REGISTRY SUB=L7 SSS FUL L9

=>

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=> FIL CAPLUS
FILE 'CAPLUS' ENTERED AT 17:28:17 ON 25 APR 96
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COPYRIGHT (C) 1996 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1967 - 25 Apr 1996  VOL 124 ISS 18
FILE LAST UPDATED: 25 Apr 1996  (960425/ED)

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  Thesauri are now available for the WIPO International Patent
  Classifications (IPC) editions 1-6 in the /IC1, /IC2, /IC3, /IC4,
  /IC5, and /IC (/IC6) fields, respectively.  The thesauri in the
  /IC5 and /IC fields also include the corresponding catchword terms
  from the IPC subject headings and subheadings.

=> S L10
L11           5 L10
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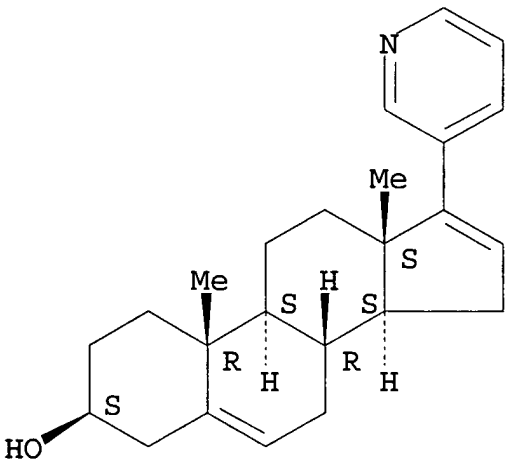
=> D BIB ABS HITSTR

L11 ANSWER 1 OF 5 CAPLUS COPYRIGHT 1996 ACS
AN 1995:874329 CAPLUS
DN 123:329474
TI Active-site conformation of 17-(3-pyridyl)androsta-5,16-dien-3.beta.-ol, a potent inhibitor of the P450 enzyme C17.alpha.-hydroxylase/C17-20 lyase
AU Burke, David F.; Laughton, Charles A.; Snook, Chris F.; Neidle, Stephen
CS Cancer Research Campaign Biomolecular Structure Unit, Institute Cancer Research, Sutton, Surrey, SM2 5NG, UK
SO Bioorg. Med. Chem. Lett. (1995), 5(11), 1125-30
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
AB 17-(3-Pyridyl)androsta-5,16-dien-3.beta.-ol, a nanomolar inhibitor of the P 450 enzyme C17.alpha.-hydroxylase/C17-20 lyase, is a target for prostate cancer chemotherapy. A model is presented for the inhibitor docked into the structure of the enzyme.
IT **154229-19-3**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(active-site conformation of 17-(3-pyridyl)androsta-5,16-dien-3.beta.-ol, a potent inhibitor of the P 450 enzyme C17.alpha.-hydroxylase/C17-20 lyase)
RN 154229-19-3 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(3-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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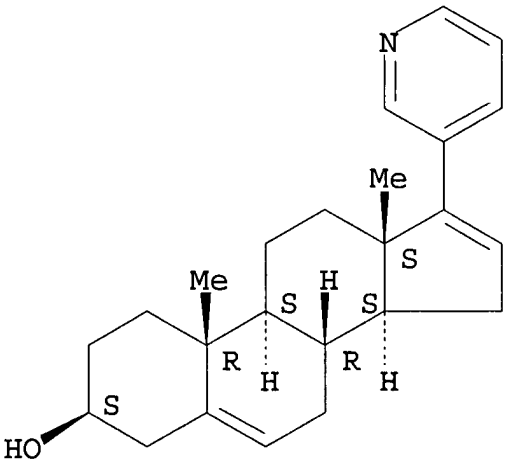
L11 ANSWER 2 OF 5 CAPLUS COPYRIGHT 1996 ACS
AN 1995:723267 CAPLUS
DN 123:112515
TI Synthesis of 17-(3-pyridyl) steroids
IN Potter, Gerard Andrew; Hardcastle, Ian Robert
PA British Technology Group Ltd., UK
SO Brit. UK Pat. Appl., 17 pp.
CODEN: BAXXDU
PI GB 2282377 A1 950405
AI GB 94-19139 940922
PRAI GB 93-20132 930930
GB 94-14192 940714
DT Patent
LA English
OS CASREACT 123:112515; MARPAT 123:112515
AB 17-(3-Pyridinyl)-substituted steroids are prepd. by subjecting a 17-iodo or -bromo steroid to a palladium complex-catalyzed cross-coupling reaction with a (3-pyridyl)-substituted borane in a proportion of at least 1.0 equiv. of borane per equiv. of steroid, in an org. solvent, and optionally esterifying the resulting 3.beta.-hydroxy steroid. Thus, dehydroepiandrosterone was converted to its hydrazone and then to its iodide. The latter compd. was treated with 1.1 equiv. diethyl(3-pyridyl)borane and then acetylated to give 3.beta.-acetoxy-17-(3-pyridyl)androsta-5,16-diene.
IT **154229-19-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 17-(3-pyridyl) steroids)
RN 154229-19-3 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(3-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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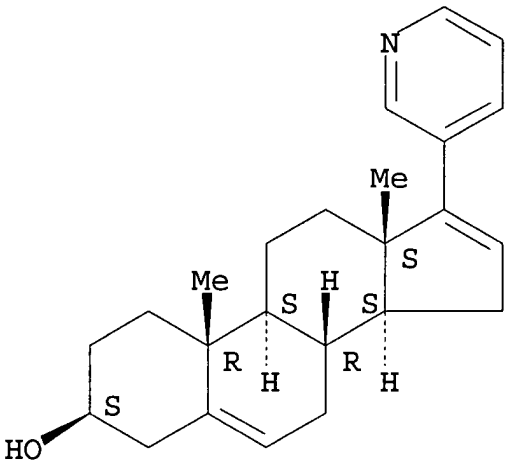
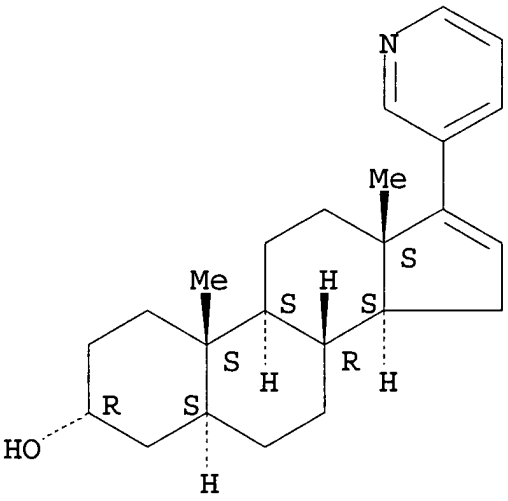
L11 ANSWER 3 OF 5 CAPLUS COPYRIGHT 1996 ACS
AN 1995:608136 CAPLUS
DN 123:83811
TI Novel Steroidal Inhibitors of Human Cytochrome P45017.alpha.-Hydroxylase-C17,20-lyase): Potential Agents for the Treatment of Prostatic Cancer
AU Potter, Gerard A.; Barrie, S. Elaine; Jarman, Michael; Rowlands, Martin G.
CS Cancer Research Campaign Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton/Surrey, SM2 5NG, UK
SO J. Med. Chem. (1995), 38(13), 2463-71
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CJACS-IMAGE; CJACS
AB Steroidal compds. having a 17-(3-pyridyl) substituent together with a 16,17-double bond have been synthesized using a palladium-catalyzed cross-coupling reaction of a 17-enol triflate with diethyl(3-pyridyl)borane and are potent inhibitors of human testicular 17.alpha.-hydroxylase-C17,20-lyase. The requirement for these structural features is stringent: compds. having 2-pyridyl, 4-pyridyl, or 2-pyridylmethyl substituents instead of 3-pyridyl substituents were either poor inhibitors or noninhibitory. Redn. of the 16,17-double bond to give 17.beta.-pyridyl derivs. diminished potency with 3-pyridyl substitution, but increased it with a 4-pyridyl substituent present. In contrast, a variety of substitution patterns in rings A-C of the steroid skeleton was tolerated. The most potent compds. are candidates for development as drugs for the treatment of hormone-dependent prostatic carcinoma.
IT **154229-19-3P 154229-25-1P 165334-72-5P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of novel steroidal inhibitors of human cytochrome P 45017.alpha.-hydroxylase-C17,20-lyase)
RN 154229-19-3 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(3-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



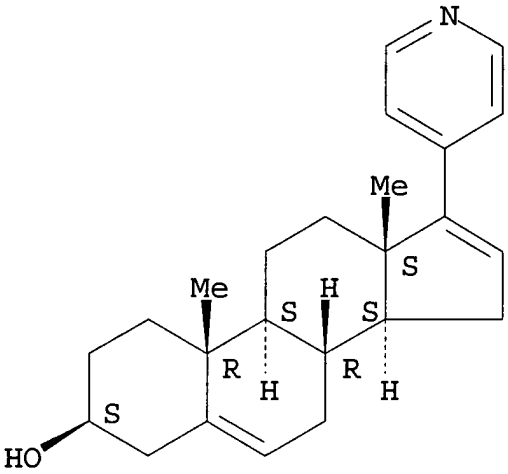
RN 154229-25-1 CAPLUS
CN Androst-16-en-3-ol, 17-(3-pyridinyl)-, (3.alpha.,5.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



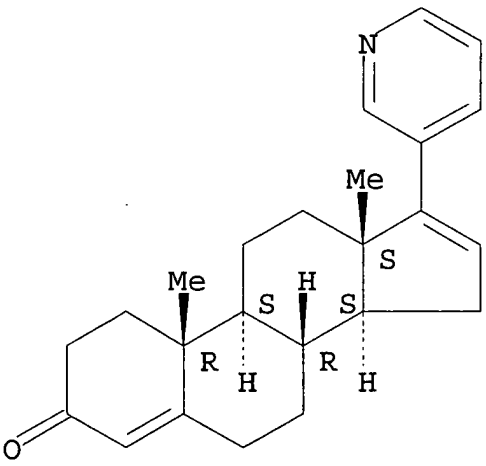
RN 165334-72-5 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(4-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



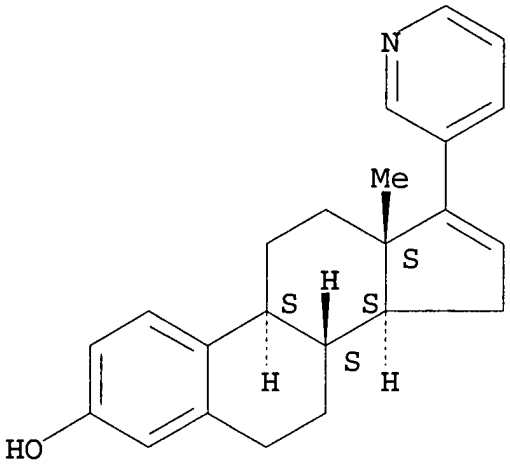
IT **154229-21-7P 154229-23-9P 154229-26-2P**
154229-27-3P 165334-71-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of novel steroidal inhibitors of human cytochrome P 45017.alpha.-hydroxylase-C17,20-lyase)
RN 154229-21-7 CAPLUS
CN Androsta-4,16-dien-3-one, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



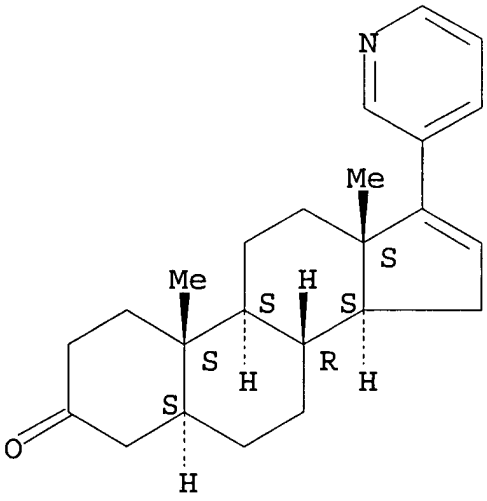
RN 154229-23-9 CAPLUS
CN Estra-1,3,5(10),16-tetraen-3-ol, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



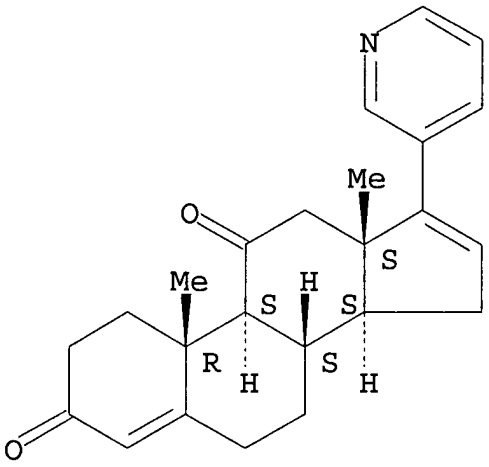
RN 154229-26-2 CAPLUS
CN Androst-16-en-3-one, 17-(3-pyridinyl)-, (5.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



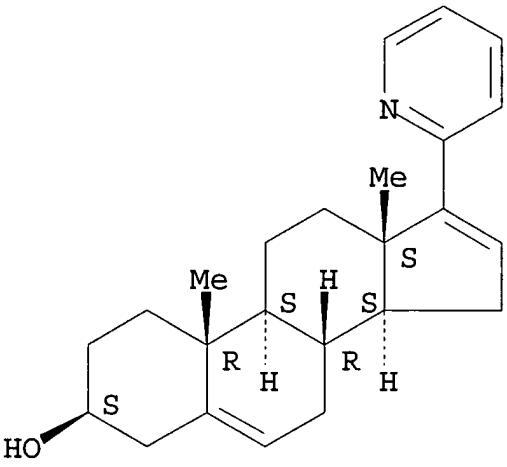
RN 154229-27-3 CAPLUS
CN Androsta-4,16-diene-3,11-dione, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 165334-71-4 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(2-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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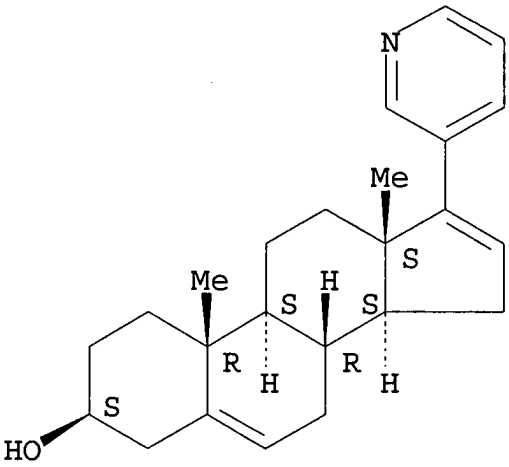
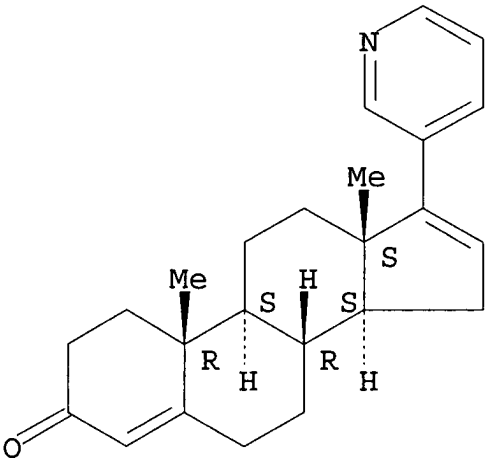
L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 1996 ACS
AN 1994:645446 CAPLUS
DN 121:245446
TI Pharmacology of novel steroidal inhibitors of cytochrome P45017.alpha. (17.alpha.-hydroxylase/C17-20 lyase)
AU Barrie, S. E.; Potter, G. A.; Goddard, P. M.; Haynes, B. P.; Dowsett, M.; Jarman, M.
CS Drug Development Sec., Inst. Cancer Res., Sutton, SM2 5NG, UK
SO J. Steroid Biochem. Mol. Biol. (1994), 50(5-6), 267-73
CODEN: JSBBEZ; ISSN: 0960-0760
DT Journal
LA English
AB Medical or surgical castration for the treatment of prostatic cancers prevents androgen prodn. by the testes, but not by the adrenals. Inhibition. of the key enzyme for androgen biosynthesis, cytochrome P 45017.alpha., could prevent androgen prodn. from both sources. The in vivo effects of 17-(3-pyridyl)androsta-5,16-dien-3.beta.-ol (CB7598) and 17-(3-pyridyl)androsta-5,16-dien-3-one (CB7627), novel potent steroidal inhibitors of this enzyme, on WHT mice were compared with those of castration and two clin. active compds., ketoconazole and flutamide. Flutamide and surgical castration caused significant redns. in the wts. of the ventral prostate and seminal vesicles. CB7598, in its 3.beta.-O-acetate form (CB7630), and CB7627 caused significant redns. in the wts. of the ventral prostate, seminal vesicles, kidneys and testes when administered once daily for 2 wks. Ketoconazole, given on the same schedule, caused no redns. Plasma testosterone was reduced to .ltoreq. 0.1 nM by CB7630, despite a 3- to 4-fold increase in the plasma level of LH. Adrenal wts. were unchanged following treatment with CB7630 or CB7627 but were markedly increased following ketoconazole, indicating no inhibition. of corticosterone prodn. by these steroidal compds. These results indicate that CB7598, CB7630 or CB7627 may be useful in the treatment of hormone-dependent prostatic cancers.
IT **154229-19-3**, CB 7598 **154229-21-7**, CB 7627
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of steroidal inhibitors of cytochrome P 45017.alpha. (17.alpha.-hydroxylase/C17-20 lyase))
RN 154229-19-3 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(3-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



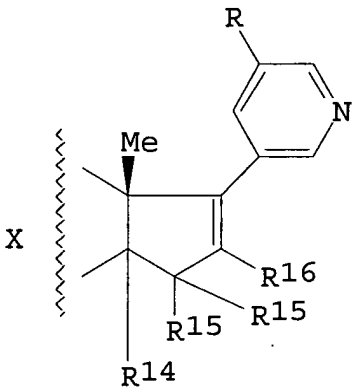
RN 154229-21-7 CAPLUS
CN Androsta-4,16-dien-3-one, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> D BIB ABS HITSTR 5

L11 ANSWER 5 OF 5 CAPLUS COPYRIGHT 1996 ACS
AN 1994:270958 CAPLUS
DN 120:270958
TI 17-(3-Pyridyl)-substituted steroids useful in cancer treatment
IN Barrie, Susan Elaine; Jarman, Michael; Potter, Gerard Andrew
PA British Technology Group Ltd., UK
SO Brit. UK Pat. Appl., 40 pp.
CODEN: BAXXDU
PI GB 2265624 A1 931006
AI GB 93-5269 930315
PRAI GB 92-7057 920331
GB 92-24880 921127
DT Patent
LA English
OS MARPAT 120:270958
GI



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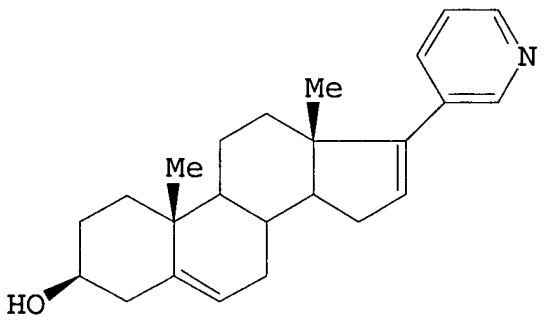


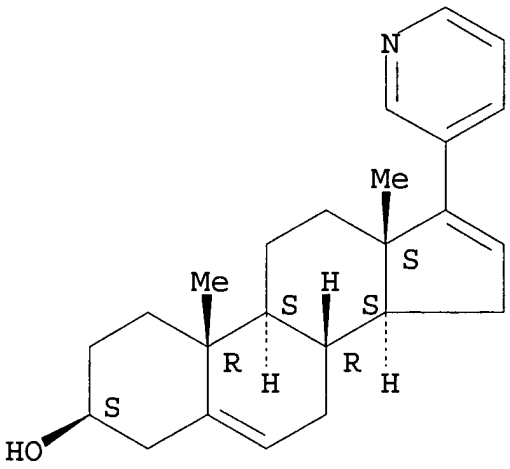
II

AB The title compds. are useful for treatment of androgen-dependent disorders, esp. prostatic cancer, and also estrogen-dependent disorders such as breast cancer. Claimed are compds. of formula I [X = steroid A-B-C ring residue; R = H, alkyl; R14 = H, halo, alkyl; R15 = H, alkyl, alkoxy, OH, alkylcarbonyloxy; or R15R15 = oxo, CH2; or R14R15 = pi bond and the other R15 = H, alkyl; R16 = H, halo, alkyl], in the form of free bases or pharmaceutically acceptable acid addn. salts, with the proviso that 5 specific compds. are claimed only for use in therapy. For example, dehydroepiandrosterone 3-acetate [i.e. 3.beta.-acetoxyandrost-5-en-17-one] was treated with (CF3SO2)2O and 2,6-di-tert-butyl-4-methylpyridine in CH2Cl2 to give 58% androsta-3,5,16-trien-17-yl trifluoromethanesulfonate. This triflate was coupled with diethyl(3-pyridyl)borane in the presence of Pd(PPh3)2Cl2 (84%), followed by hydrolytic deacetylation with aq. NaOH (79%), to give pyridylandrostadienol II. The IC50 values of II for inhibition of C17-C20 lyase and 17.alpha.-hydroxylase in vitro were, resp., 0.0029 .mu.M and 0.0040 .mu.M (cf. 0.026 and 0.065 for ketoconazole). In vivo organ wt. and endocrine test results for appropriate I in mice indicated inhibition of androgen synthesis, particularly testosterone.

IT **154229-19-3P 154229-21-7P 154229-23-9P**

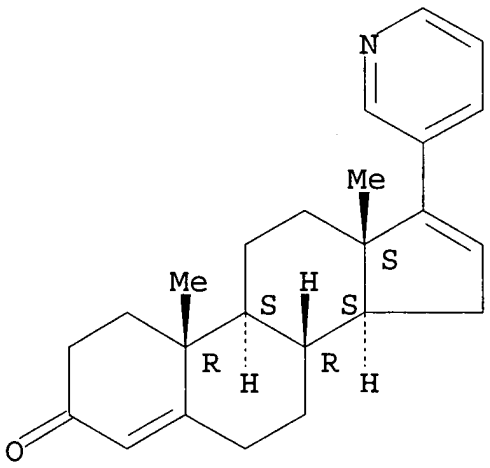
154229-25-1P 154229-26-2P 154229-27-3P
154229-29-5P 154229-30-8P 154229-33-1P
154229-34-2P 154229-35-3P 154229-47-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of hormone-dependent cancer)
RN 154229-19-3 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(3-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



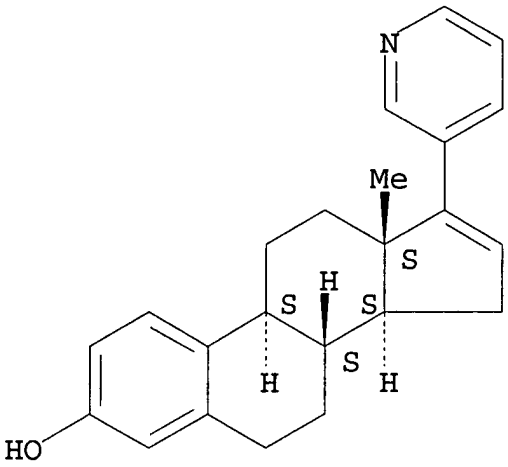
RN 154229-21-7 CAPLUS
CN Androsta-4,16-dien-3-one, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154229-23-9 CAPLUS
CN Estra-1,3,5(10),16-tetraen-3-ol, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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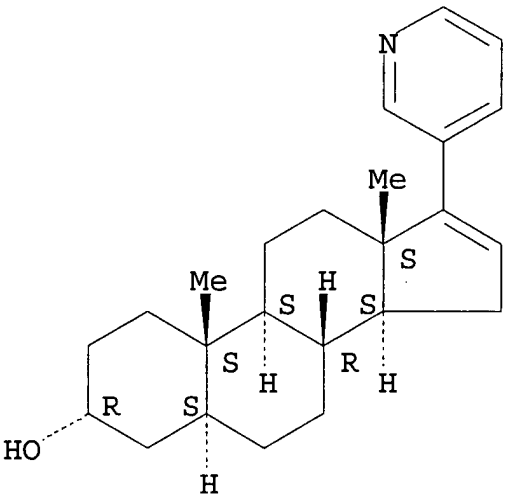
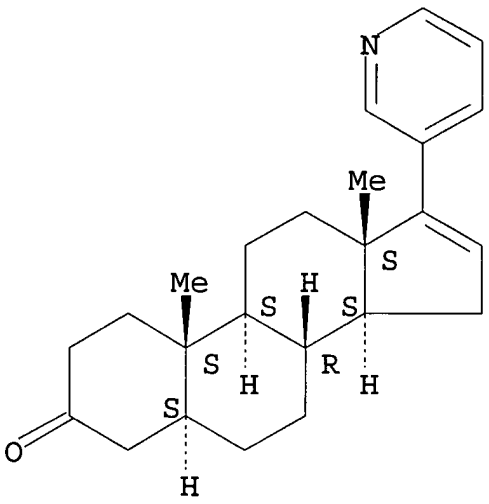
CN Androst-16-en-3-ol, 17-(3-pyridinyl)-, (3.alpha.,5.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154229-26-2 CAPLUS
CN Androst-16-en-3-one, 17-(3-pyridinyl)-, (5.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154229-27-3 CAPLUS
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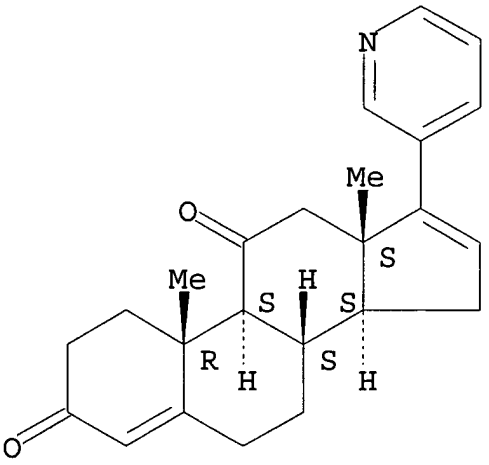
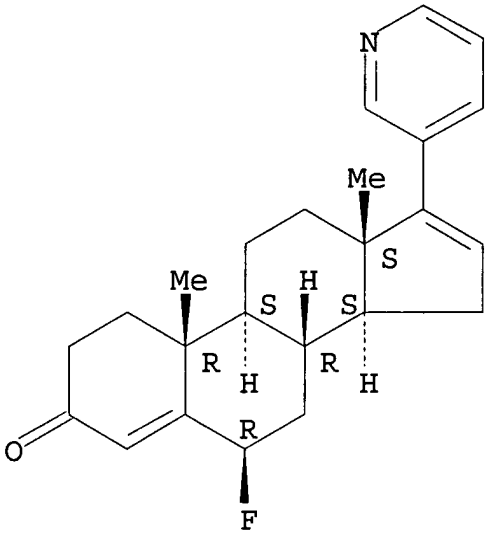
Absolute stereochemistry.



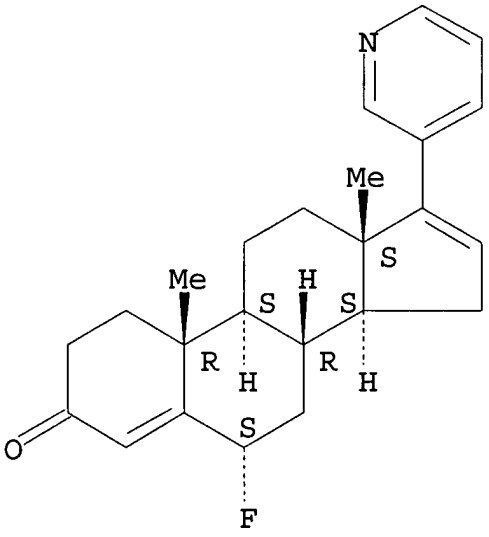
RN 154229-29-5 CAPLUS
CN Androsta-4,16-dien-3-one, 6-fluoro-17-(3-pyridinyl)-, (6.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



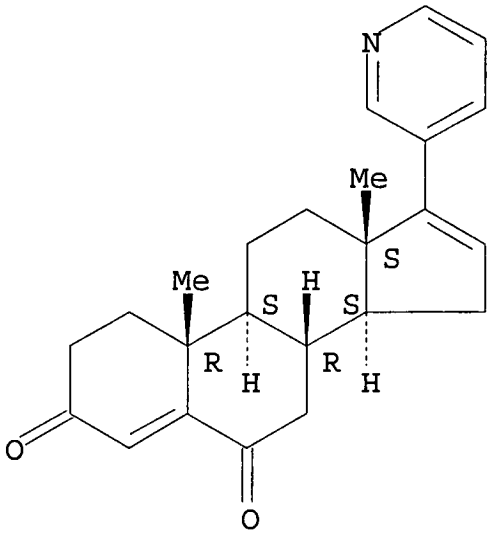
RN 154229-30-8 CAPLUS
CN Androsta-4,16-dien-3-one, 6-fluoro-17-(3-pyridinyl)-, (6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



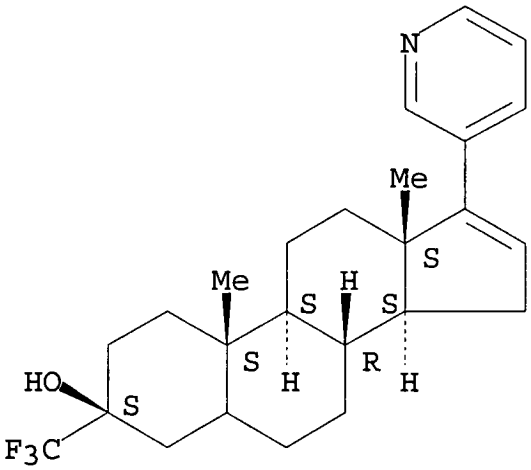
RN 154229-33-1 CAPLUS
CN Androsta-4,16-diene-3,6-dione, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



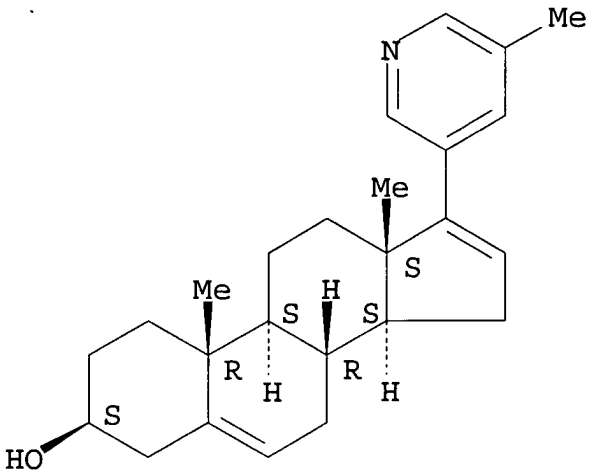
RN 154229-34-2 CAPLUS
CN Androst-16-en-3-ol, 17-(3-pyridinyl)-3-(trifluoromethyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



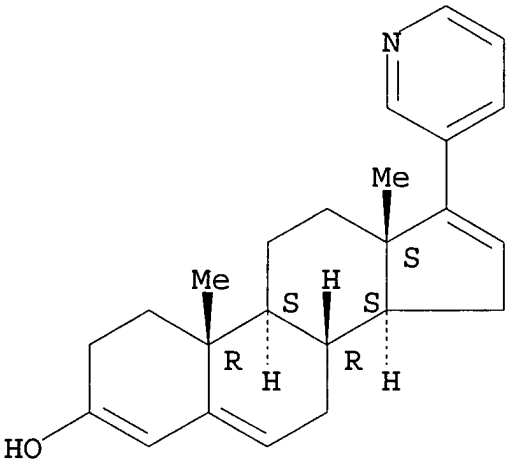
RN 154229-35-3 CAPLUS
CN Androsta-5,16-dien-3-ol, 17-(5-methyl-3-pyridinyl)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



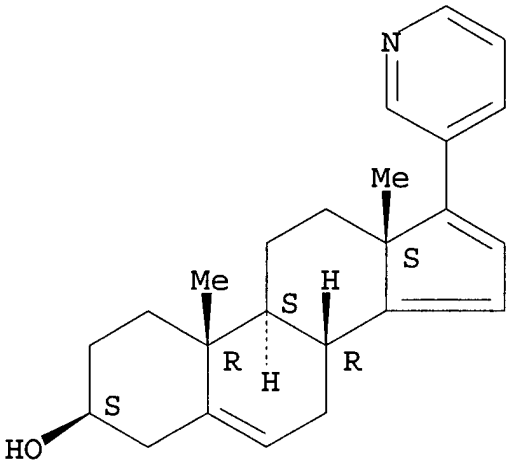
RN 154229-47-7 CAPLUS
CN Androsta-3,5,16-trien-3-ol, 17-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



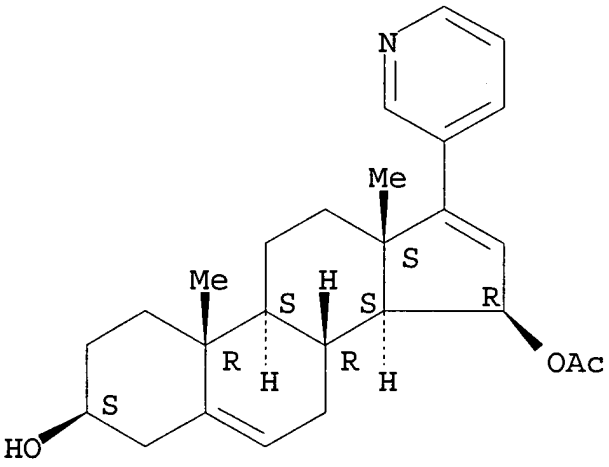
IT **154229-45-5 154229-46-6**
RL: RCT (Reactant)
(therapeutic use of)
RN 154229-45-5 CAPLUS
CN Androsta-5,14,16-trien-3-ol, 17-(3-pyridinyl)-, (3.beta.)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 154229-46-6 CAPLUS
CN Androsta-5,16-diene-3,15-diol, 17-(3-pyridinyl)-, 15-acetate, (3.beta.,15.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> FIL CAOLD
FILE 'CAOLD' ENTERED AT 17:29:11 ON 25 APR 96
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 1996 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1957-1966
FILE LAST UPDATED:  30 OCT 91 (910803/ED)

  To help control your online searching costs, consider using the
  HCAOLD  File when conducting SmartSELECT searches with large
  numbers of terms.

=> D HIS

     (FILE 'HOME' ENTERED AT 17:21:55 ON 25 APR 96)

     FILE 'REGISTRY' ENTERED AT 17:21:59 ON 25 APR 96
L1              STR
L2           25 S L1
L3              STR L1
L4           35 S L3
L5              STR L3
L6            6 S L5
L7          129 S L5 FUL

     FILE 'CAPLUS' ENTERED AT 17:27:07 ON 25 APR 96
L8           19 S L7

     FILE 'REGISTRY' ENTERED AT 17:27:14 ON 25 APR 96
L9              STR L5
L10          16 S L9 SSS FUL SUB=L7

     FILE 'REGISTRY' ENTERED AT 17:28:07 ON 25 APR 96

     FILE 'CAPLUS' ENTERED AT 17:28:17 ON 25 APR 96
L11           5 S L10

     FILE 'CAOLD' ENTERED AT 17:29:11 ON 25 APR 96
L12           0 S L10

     FILE 'BEILSTEIN' ENTERED AT 17:29:21 ON 25 APR 96
L13           0 S L9 FUL

     FILE 'MARPAT' ENTERED AT 17:29:43 ON 25 APR 96
L14           6 S L7 FUL
L15           3 S L9 SSS FUL SUB=L14

=>
=>
=> D QUE L15
L5              STR
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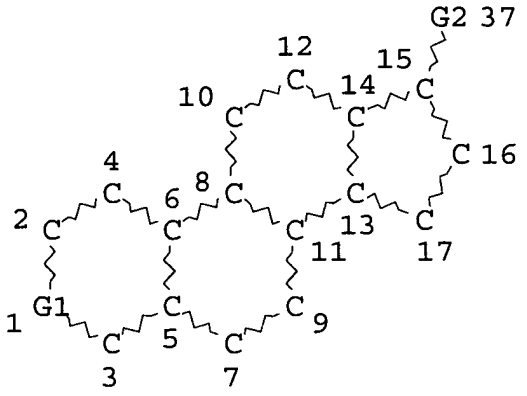
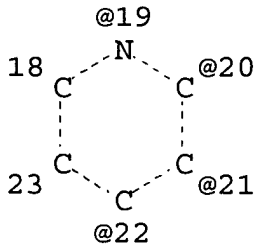


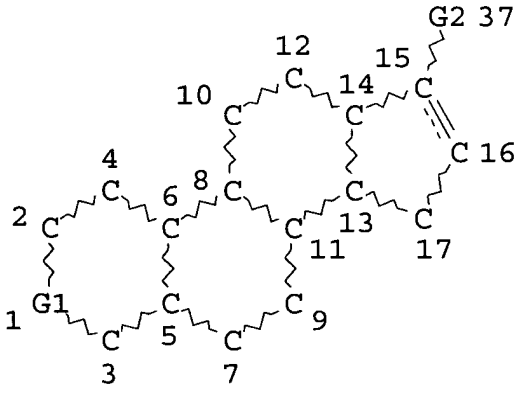


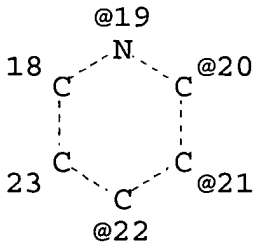
CH2=C 26 @27 O~C 29 @30 NC~C 32 @33 O2N~C 35 @36

VAR G1=27/30/33/36
VAR G2=19/20/21/22
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L9 STR





CH2=C 26 @27 O~C 29 @30 NC~C 32 @33 O2N~C 35 @36

VAR G1=27/30/33/36
VAR G2=19/20/21/22
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 29
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

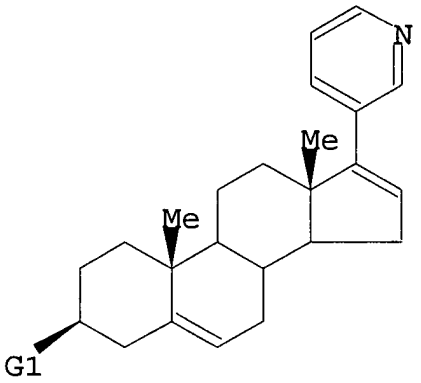
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L14 6 SEA FILE=MARPAT SSS FUL L5
L15 3 SEA FILE=MARPAT SUB=L14 SSS FUL L9

=> D QHIT BIB ABS

L15 ANSWER 1 OF 3 MARPAT COPYRIGHT 1996 ACS

MSTR 3



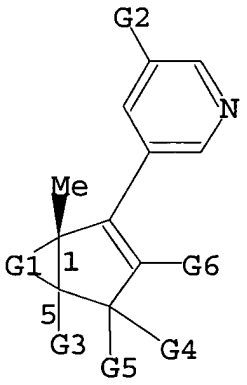
G1 = OH
MPL: disclosure

AN 123:112515 MARPAT
TI Synthesis of 17-(3-pyridyl) steroids
IN Potter, Gerard Andrew; Hardcastle, Ian Robert
PA British Technology Group Ltd., UK
SO Brit. UK Pat. Appl., 17 pp.
CODEN: BAXXDU
PI GB 2282377 A1 950405
AI GB 94-19139 940922
PRAI GB 93-20132 930930
GB 94-14192 940714
DT Patent
LA English
OS CASREACT 123:112515
AB 17-(3-Pyridinyl)-substituted steroids are prepd. by subjecting a 17-iodo or -bromo steroid to a palladium complex-catalyzed cross-coupling reaction with a (3-pyridyl)-substituted borane in a proportion of at least 1.0 equiv. of borane per equiv. of steroid, in an org. solvent, and optionally esterifying the resulting 3.beta.-hydroxy steroid. Thus, dehydroepiandrosterone was converted to its hydrazone and then to its iodide. The latter compd. was treated with 1.1 equiv. diethyl(3-pyridyl)borane and then acetylated to give 3.beta.-acetoxy-17-(3-pyridyl)androsta-5,16-diene.

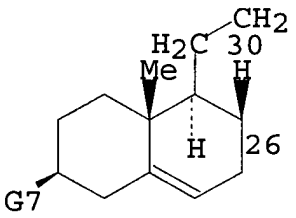
=> D QHIT BIB ABS 2

L15 ANSWER 2 OF 3 MARPAT COPYRIGHT 1996 ACS

MSTR 1

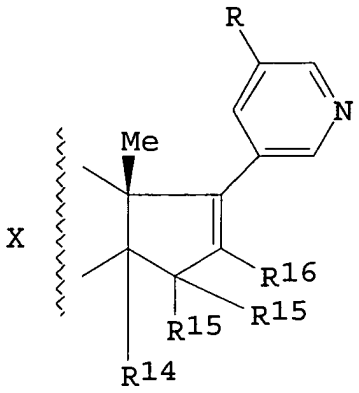


G1 = 30-1 26-5

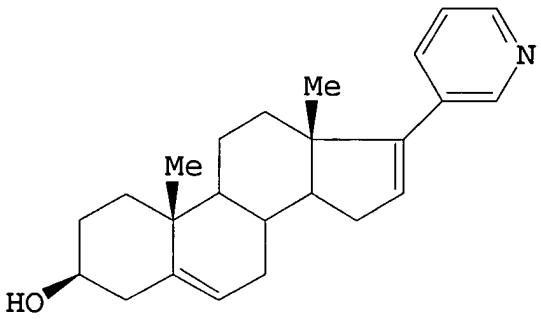


G7 = OH
DER: or steroid derivatives
MPL: claim 1
NTE: substitution is restricted

AN 120:270958 MARPAT
TI 17-(3-Pyridyl)-substituted steroids useful in cancer treatment
IN Barrie, Susan Elaine; Jarman, Michael; Potter, Gerard Andrew
PA British Technology Group Ltd., UK
SO Brit. UK Pat. Appl., 40 pp.
CODEN: BAXXDU
PI GB 2265624 A1 931006
AI GB 93-5269 930315
PRAI GB 92-7057 920331
GB 92-24880 921127
DT Patent
LA English
GI



I



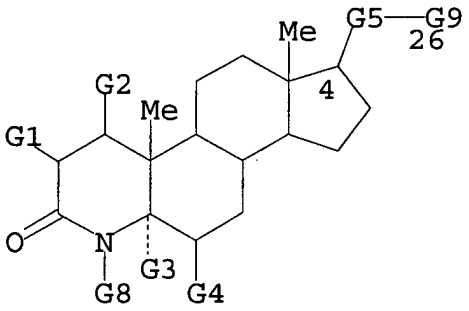
II

AB The title compds. are useful for treatment of androgen-dependent disorders, esp. prostatic cancer, and also estrogen-dependent disorders such as breast cancer. Claimed are compds. of formula I [X = steroid A-B-C ring residue; R = H, alkyl; R14 = H, halo, alkyl; R15 = H, alkyl, alkoxy, OH, alkylcarbonyloxy; or R15R15 = oxo, CH2; or R14R15 = pi bond and the other R15 = H, alkyl; R16 = H, halo, alkyl], in the form of free bases or pharmaceutically acceptable acid addn. salts, with the proviso that 5 specific compds. are claimed only for use in therapy. For example, dehydroepiandrosterone 3-acetate [i.e. 3.beta.-acetoxyandrost-5-en-17-one] was treated with (CF3SO2)2O and 2,6-di-tert-butyl-4-methylpyridine in CH2Cl2 to give 58% androsta-3,5,16-trien-17-yl trifluoromethanesulfonate. This triflate was coupled with diethyl(3-pyridyl)borane in the presence of Pd(PPh3)2Cl2 (84%), followed by hydrolytic deacetylation with aq. NaOH (79%), to give pyridylandrostadienol II. The IC50 values of II for inhibition of C17-C20 lyase and 17.alpha.-hydroxylase in vitro were, resp., 0.0029 .mu.M and 0.0040 .mu.M (cf. 0.026 and 0.065 for ketoconazole). In vivo organ wt. and endocrine test results for appropriate I in mice indicated inhibition of androgen synthesis, particularly testosterone.

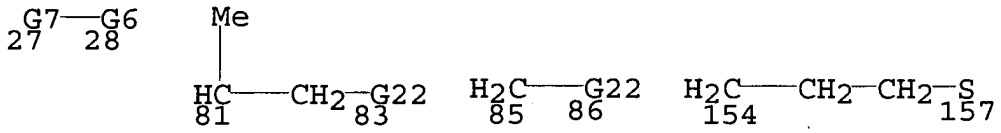
=> D QHIT BIB ABS 3

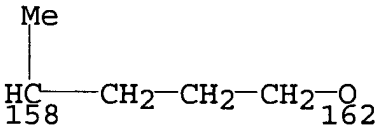
L15 ANSWER 3 OF 3 MARPAT COPYRIGHT 1996 ACS
(ALL HITs ARE ITERATION INCOMPLETES)

MSTR 1 ITERATION INCOMPLETE

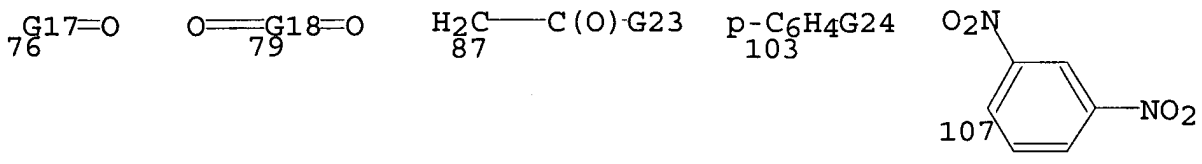


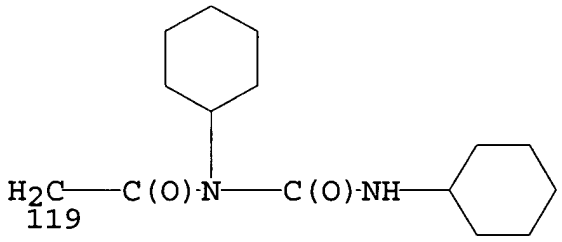
G1 = H
G2 = H
G3 = H
G4 = H
G5 = O / S / S(O) / SO2 / 27-4 28-26 / (SC 81-4 83-26 / 85-4 86-26 / 154-4 157-26 / 158-4 162-26)

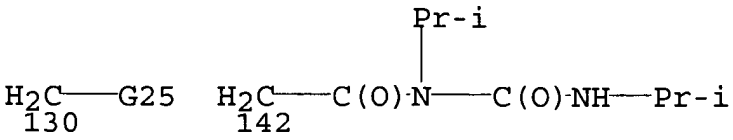


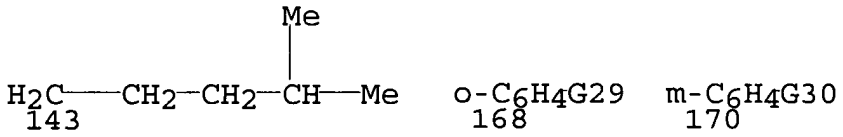


G6 = O / S / S(O) / SO2
G7 = alkylene (SO G11)
G8 = H / Me / Et / OH / NH2 / SMe
G9 = alkyl<(1-20)> (SO (1-) G10) / Ph (SO) / naphthyl (SO) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / 76 / 79 / Hy<EC (1-

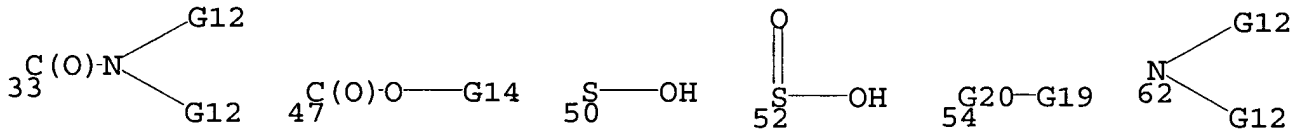


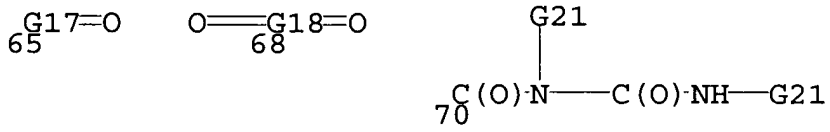






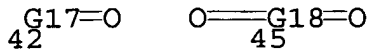
G10 = OH / F / Cl / Br / I / alkoxy<(1-8)> / alkenyl<(2-10)> / 33 / 47 / SH / 50 / 52 / 54) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / 76 / 79 / Hy<EC (1-



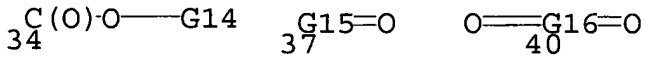


G11 = Ph / naphthyl

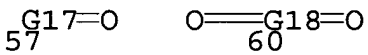
G12 = Ph / naphthylV / alkoxy<(1-8)> / alkenyl<(2-10)> / 33 / 47 / SH / 50 / 52 / 54) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / 76 / 79 / Hy<EC (1-



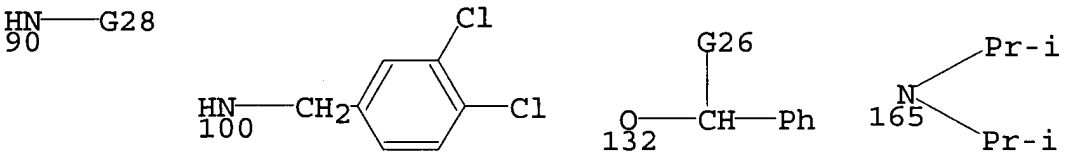
G13 = OH / alkoxy<(1-3)> / CN / 34 / NO2 / F / Cl / Br / I / N10)> / 33 / 47 / SH / 50 / 52 / 54) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / 76 / 79 / Hy<EC (1-



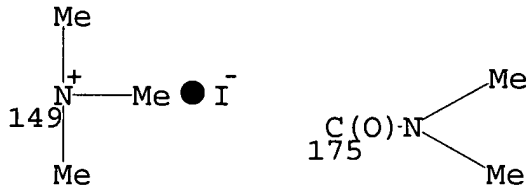
G14 = H / alkyl<(1-8)> (SO) / Ph (SO) / naphthyl (SO)
G15 = Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ (6-) C, AR (1-), BD (6-) N, RC (2), RS (0-) E5 (1-) E6 (0-) E7 (0) OTHER>
G16 = Hy<EC (1-3) Q (0-) N (0-) O (1-) S (0) OTHERQ, AN (1-) S, RC (1), RS (1) M5 (1) X7> / Hy<EC (1-3) Q (0-) N (0-) O (1-) S (0) OTHERQ (6-) C, AN (1-) S, AR (1-), BD (6-) N, RC (2), RS (0-) E5 (1-) E6 (0-) E7 (0) OTHER>
G17 = Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ, RC (1), RS (1) M5 (1) X7> (SO) / Hy<EC (1-3) Q (0-) N (0-) O (0-) S (0) OTHERQ (6-) C, AR (1-), BD (6-) N, RC (2), RS (0-) E5 (1-) E6 (0-) E7 (0) OTHER> (SO)
G18 = Hy<EC (1-3) Q (0-) N (0-) O (1-) S (0) OTHERQ, AN (1-) S, RC (1), RS (1) M5 (1) X7> (SO) / Hy<EC (1-3) Q (0-) N (0-) O (1-) S (0) OTHERQ (6-) C, AN (1-) S, AR (1-), BD (6-) N, RC (2), RS (0-) E5 (1-) E6 (0-) E7 (0) OTHER> (SO)
G19 = Hy<EC (1-3) Q (0-) N (0-) O (1-) S (0) OTHERQ, AN (1-) S, RC (1), RS (1) M5 (1) X7> (SO) / Hy<EC (1-3) Q (0-) N (0-) O (1-) S (0) OTHERQ (6-) C, AN (1-) S, AR (1-), BD (6-) N, RC (2), RS (0-) E5 (1-) E6 (0-) E7 (0) OTHER> (SO)



G20 = S / S(O) / SO2
G21 = H / alkyl<(1-8)> / CH2Ph / cyclohexyl
G22 = O / S
G23 = 132 / 90 / OH / OEt / 100 / NHPh / NH2 / 165



G24 = Ph / NO2 / NH2 / NHCOMe / CN / CONH2 / NMe2 / 149 / OMe / 175



G25 = 2-pyridyl / Ph
G26 = H / Ph
G27 = COMe / CH(OH)Me / Bu-t
G28 = 91 / 1-adamantyl / Bu-i / CH2CH2OH

G29 = CN / NO2 / CONH2
G30 = CN / CONH2
G1 +G2 = NULL
G3 +G4 = NULL
DER: or pharmaceutically acceptable salts or esters
MPL: claim 1
NTE: substitution is restricted

AN 120:245602 MARPAT
TI Preparation of 17-ethers and thioethers of 4-aza-steroids as steroid reductase inhibitors
IN Witzel, Bruce E.; Tolman, Richard L.; Rasmusson, Gary H.; Bakshi, Raman K.; Yang, Shu Shu
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
PI WO 9323040 A1 931125
DS W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 93-US4746 930519
PRAI US 92-886031 920520
DT Patent
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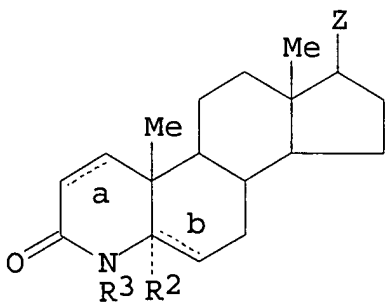

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AB Title compds. [I; a, b both = single bonds, and R2 = H; or a = double bond, b = single bond, and R2 = H; or a = single bond, b = double bond, and R2 = null; R1 = H, aryl, (aryl)alkyl; R3 = H, Me, Et, OH, NH2, SMe; R4 = (substituted) alkyl, aryl, heterocyclyl; Z = XR4, (CHR1)nXR4; X = O, S, SO, SO2], were prepd. as inhibitors of steroid 5.alpha.-reductase enzymes 1 and 2 (no data). The compds. are useful for the treatment of hyperandrogenic disease conditions and diseases of the skin and scalp. Thus, 17-hydroxymethyl-4-methyl-5.alpha.-4-azaandrostan-3-one and diphenyldiazomethane in CH2Cl2 were treated dropwise with BF3.Et2O to give 17-diphenylmethoxymethyl-4-methyl-5.alpha.-4-azaandrostan-3-one.

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(FILE 'HOME' ENTERED AT 17:21:55 ON 25 APR 96)

FILE 'REGISTRY' ENTERED AT 17:21:59 ON 25 APR 96
L1 STR
L2 25 S L1
L3 STR L1
L4 35 S L3
L5 STR L3
L6 6 S L5
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L8 19 S L7

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FILE 'BEILSTEIN' ENTERED AT 17:29:21 ON 25 APR 96
L13 0 S L9 FUL

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L15 3 S L9 SSS FUL SUB=L14

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